Cabozantinib (cabo) inhibits MET & VEGFR2. In a phase 2 NRE cohort of patients (pts) with mCRPC, cabozantinib at 100 mg daily was associated with high rates of bone scan resolution, pain relief & overall disease control, independent of PSA changes. We now report the activity & safety of cabozantinib 40 mg daily.

**Methods**

Docetaxel (D)-pretreated (≥225 mg/m²) CRPC pts with bone metastasis were required to have progressed within 6 months of last dose of D. Tumor response was assessed q6 wks. Bone scan response used computer-aided assessment of bone scan lesion area (BSLA). Diffusion Weighted MRI was performed in some pts. Pain intensity (worst pain over the past 24 hrs; BPI scale 0-10) & interference with sleep & daily activity were prospectively assessed using an IVR system (7 day intervals). Analgesic use was collected by diary. Bone turnover markers & circulating tumor cells (CTCs) were assessed.

**Results**

51 pts were enrolled. Among 30 pts who had ≥6 wks f/u, the median age was 66 yrs. 20% received cabazitaxel, 70% abiraterone, & 20% had visceral disease. 47% (14/30) had pain (BPI ≥4) at baseline (bsl) of which 86% (12/14) were using narcotics. Median bsl CTC count was 17 & 73% had ≥5. Median f/u was 84 days (range, 44-141). 55% (11/20 pts) with a f/u bone scan showed BSLA reduction (range, 1-70%). Increases in Apparent Diffusion Coefficient (suggestive of tumor necrosis) & enhancement reduction were observed in bone & soft tissue metastases. 10/14 pts (71%) evaluable for pain response had a ≥30% reduction from bsl; 7/12 (58%) pts decreased narcotics. Sleep & daily activity improved in pts with pain relief. Among pts with elevated bsl serum levels of CTx, NTx & bALP, 57%, 60% & 33% respectively, had declines ≥30%. In 22 pts with CTCs ≥5, 59% had a decrease of ≥30% at wks 6 or 12, & 23% converted to <5 CTCs. 5 (17%) pts required a dose reduction. The most common Gr 3/4 AEs were hypertension (13%), decreased appetite (7%), & back pain (7%).

**Conclusions**

Cabozantinib 40 mg was well tolerated & demonstrated bone scan resolution, substantial pain relief with a narcotic sparing effect, & reductions in bone turnover markers & CTCs in heavily pretreated mCRPC pts. MRI results are consistent with an anti-tumor effect.

**Disclosure**

M.R. Smith: Consultant to Exelixis.
O.A. Sartor: Consultant for Exelixis.

All other authors have declared no conflicts of interest.

Session Info: Proffered Papers, [] Genitourinary tumors, prostate I
Day/Date: Sunday, September 30, 2012
Session Time: 10:45 AM - 12:15 PM
Room: Hall D